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L1	maritima and chatterjee.in.	15	L1

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L12 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:761460 CAPLUS
DOCUMENT NUMBER: 132:9599
TITLE: Detection of nucleic acids by multiple sequential invasive cleavages
INVENTOR(S): Hall, Jeff G.; Lyamichev, Victor I.; Mast, Andrea L.; Brow, Mary Ann D.
PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA
SOURCE: U.S., 306 pp., Cont.-in-part of U.S. Ser. No. 759,038.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5994069	A	19991130	US 1997-823516	19970324
US 5846717	A	19981208	US 1996-599491	19960124
US 6001567	A	19991214	US 1996-682853	19960712
US 5985557	A	19991116	US 1996-756386	19961129
US 6090606	A	20000718	US 1996-758314	19961202
US 6090543	A	20000718	US 1996-759038	19961202
WO 9727214	A1	19970731	WO 1997-US1072	19970122
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
WO 9842873	A1	19981001	WO 1998-US5809	19980324
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9868690	A1	19981020	AU 1998-68690	19980324
AU 738849	B2	20010927		
EP 994964	A1	20000426	EP 1998-914299	19980324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518805	T2	20011016	JP 1998-545934	19980324
US 6458535	B1	20021001	US 1999-350597	19990709
US 2002187486	A1	20021212	US 2001-33297	20011102

PRIORITY APPLN. INFO.:

US 1996-599491	A2	19960124
US 1996-682853	A2	19960712
US 1996-756386	A2	19961129
US 1996-758314	A2	19961202
US 1996-759038	A2	19961202
WO 1997-US1072	A2	19970122
US 1996-756038	B2	19961126
US 1996-756376	A2	19961202
US 1997-823516	A2	19970324
WO 1998-US5809	W	19980324
US 1999-350597	A1	19990709

AB The present invention relates to means for the detection and characterization of nucleic acid sequences, as well as variations in nucleic acid sequences, by an Invader.RTM. oligonucleotide-directed cleavage detection assay. The present invention also relates to methods for forming a nucleic acid cleavage structure on a target sequence and cleaving the nucleic acid cleavage structure in a site-specific manner. The structure-specific nuclease activity of a variety of enzymes is used to cleave the target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. Derivs. of thermostable **DNA polymerases** and their **mutants** that retain their 5'-nuclease activity but lack polymerase activity are described for use in the nucleic acid detection system. The nuclease activity cleaves the single-stranded moiety of a Y-shaped structure and so is of use in selected cleavage of reporter

sequences in a hybridization assay that includes 5'-nuclease-dependent cleavage and amplification steps. The present invention further relates to methods and devices for the sepn. of nucleic acid mols. based on charge. The present invention also provides methods for the detection of non-target cleavage products via the formation of a complete and activated protein binding region. The invention further provides sensitive and specific methods for the detection of human cytomegalovirus nucleic acid in a sample.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:64619 CAPLUS
DOCUMENT NUMBER: 130:121430
TITLE: **Mutant** chimeric Thermus/Tma **DNA polymerases** with improved properties for nucleic acid sequencing
INVENTOR(S): Gelfand, David Harrow; Reichert, Fred Lawrence
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 892058	A2	19990120	EP 1998-112327	19980703
EP 892058	A3	20010926		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6228628	B1	20010508	US 1998-105697	19980626
CA 2240570	AA	19990109	CA 1998-2240570	19980707
JP 11089588	A2	19990406	JP 1998-208533	19980709

PRIORITY APPLN. INFO.: US 1997-52065P P 19970709

AB The invention provides **mutant**, chimeric thermostable **DNA polymerase** enzymes consisting of an N-terminal region derived from the 5'-nuclease domain of a Thermus species **DNA polymerase** and a C-terminal region derived from the 3' to 5' exonuclease and polymerase domains of Tma **DNA polymerase**. These **mutant** chimeric thermostable **DNA polymerase** enzymes have improved properties in nucleic acid sequencing reactions. Also provided are nucleic acids encoding said **mutant** chimeric thermostable **DNA polymerase** enzymes, vectors comprising said nucleic acids and host cells transformed with said vectors. Also provided are compns. comprising said mutated, chimeric thermostable **DNA polymerase** enzymes and non-ionic polymeric detergent(s). Furthermore methods for producing the said enzymes and methods and kits for using the said enzymes are provided.

L12 ANSWER 17 OF 32 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
ACCESSION NUMBER: 1999:236361 BIOSIS
DOCUMENT NUMBER: PREV199900236361
TITLE: New reagents for directed modification of biopolymers: Photoaffinity modification of Tte **DNA polymerase**.
AUTHOR(S): Kolpashchikov, D. M.; Zakharenko, A. L.; Dezhurov, S. V.; Rechkunova, N. I.; Khodyreva, S. N.; Degtyarev, S. Kh.; Litvak, V. V.; Lavrik, O. I. (1)
CORPORATE SOURCE: (1) Siberian Division, Novosibirsk Institute of Bioorganic Chemistry, Russian Academy of Sciences, prosp. Akademika Lavrent'eva 8, Novosibirsk, 630090 Russia

SOURCE: Bioorganicheskaya Khimiya, (Feb., 1999) Vol. 25, No. 2, pp. 129-136.
ISSN: 0132-3423.
DOCUMENT TYPE: Article
LANGUAGE: Russian
SUMMARY LANGUAGE: English; Russian

AB Arylazides N-(4-azido-2,5-difluoro-3-chloropyridinyl-6)-beta-alanine (Ia) and N-(4-azido-2,5-difluoro-3-chloropyridinyl-6)-glycine (Ib) were synthesized and covalently attached to 5-(3-aminopropenyl-1)-dUTP through the amino group to give 5'-triphosphate (IIa) and 5'-triphosphate (IIb). The resulting azides were subjected to photolysis in aqueous solution. The spectral and photochemical characteristics of azides (I) and (II) imply that their use for the modification of biopolymers holds promise. Compounds (IIa, b) effectively substituted dTTP in DNA polymerization catalyzed by thermostable **DNA polymerase** from **Thermus thermophilus** B-35 (Tte **DNA polymerase**). Photoaffinity modification of Tte **DNA polymerase** was carried out by dTTP analogues (IIa, b) and by earlier obtained 5-(N-(5-azido-2-nitrobenzoyl)-trans-3-aminopropenyl-1) deoxyuridine 5'-triphosphate (III) and 5-(N-(4-azido-2,3,5,6-tetrafluorobenzoyl)-trans-3-aminopropenyl-1) deoxyuridine 5'-triphosphate (IV) using two **variants** of labeling. All four dTTP analogues were shown to modify Tte **DNA polymerase**.

L12 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:388639 CAPLUS
DOCUMENT NUMBER: 129:64906
TITLE: Invasive cleavage of nucleic acids for detecting and characterizing target nucleic acids and microbial nucleases for the methods
INVENTOR(S): Kaiser, Michael W.; Lyamichev, Victor I.; Lyamicheva, Natasha
PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA; Kaiser, Michael W.; Lyamichev, Victor I.; Lyamicheva, Natasha
SOURCE: PCT Int. Appl., 472 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823774	A1	19980604	WO 1997-US21783	19971126
W: AU, CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5843669	A	19981201	US 1996-757653	19961129
US 6090606	A	20000718	US 1996-758314	19961202
AU 9855898	A1	19980622	AU 1998-55898	19971126
AU 737449	B2	20010823		
EP 966542	A1	19991229	EP 1997-952237	19971126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001526526	T2	20011218	JP 1998-524043	19971126

PRIORITY APPLN. INFO.:
US 1996-757653 A2 19961129
US 1996-758314 A2 19961202
US 1996-599491 A2 19960124
US 1996-682853 A2 19960712
US 1996-756386 A2 19961129
US 1996-756376 A2 19961202
WO 1997-US21783 W 19971126

AB The present invention relates to means for the detection and characterization of nucleic acid sequences, as well as variations in nucleic acid sequences. The present invention also relates to improved

cleavage means for the detection and characterization of nucleic acid sequences. Structure-specific nucleases derived from a variety of thermostable organisms are provided. These structure-specific nucleases are used to cleave target-dependent cleavage structures, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. Disclosed are methods for the detection and characterization of nucleic acid sequences and their **variants** by using structure-specific 5'-nucleases derived from thermostable **DNA polymerases**, or the FEN-1, RAD2, or XPG class of nucleases. The enzyme cleaves the target nucleic acid sequence at a structure formed via annealing with 2 pilot oligonucleotide sequences. Also disclosed are methods and devices for the sepn. of nucleic acid mols. based on charge. Also disclosed are methods for the detection of non-target cleavage products via the formation of a complete and activated protein binding region. Isolation of genes for endonuclease FEN-1 from Pyrococcus woesei, Methanococcus jannaschii, Archaeoglobus fulgidus, Methanobacterium thermoautotrophicum, and Pyrococcus furiosus are described. Prepn. of 5'-nucleases by deleting the C-terminal polymerase domain or by point mutations of Taq **DNA polymerase**, and the prepn. of chimeric enzymes of the FEN-1 endonucleases are also shown. The cleavage method was used for the identification of hepatitis C virus and human ras gene.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:785600 CAPLUS
DOCUMENT NUMBER: 130:33958
TITLE: Cleavage of nucleic acid acid using thermostable Methanococcus jannaschii FEN-1 endonucleases
INVENTOR(S): Kaiser, Michael W.; Lyamichev, Victor I.; Lyamichev, Natasha
PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA
SOURCE: U.S., 330 pp., Cont.-in-part of U.S. Ser. No. 599,491.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5843669	A	19981201	US 1996-757653	19961129
US 5846717	A	19981208	US 1996-599491	19960124
WO 9823774	A1	19980604	WO 1997-US21783	19971126
W: AU, CA, JP, US, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9855898	A1	19980622	AU 1998-55898	19971126
AU 737449	B2	20010823		
EP 966542	A1	19991229	EP 1997-952237	19971126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001526526	T2	20011218	JP 1998-524043	19971126

PRIORITY APPLN. INFO.:
US 1996-599491 A2 19960124
US 1996-757653 A2 19961129
US 1996-758314 A2 19961202
WO 1997-US21783 W 19971126

AB The present invention relates to means for cleaving a nucleic acid cleavage structure in a site-specific manner. Structure-specific nucleases, including 5' nucleases, thermostable FEN-1 endonucleases and 3' exonucleases, are used to detect and identify target nucleic acids. Methods are provided which allow for the detection specific nucleic acid sequences; these methods permit the detection and identification of **mutant** and wild-type forms of genes (e.g., human genes) as well as

permit the detection and identification of bacterial and viral pathogens in a sample.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 20 OF 32 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 1998:607277 SCISEARCH
THE GENUINE ARTICLE: 106WC
TITLE: Engineering an Mg2+ site to replace a structurally conserved arginine in the catalytic center of histidyl-tRNA synthetase by computer experiments
AUTHOR: Arnez J G; Flanagan K; Moras D; Simonson T (Reprint)
CORPORATE SOURCE: UNIVERSITE LOUIS PASTEUR, CNRS, INSERM, INST GENET & BIOL MOL & CELLULAIRE, STRUCT BIOL LAB, BP 163, F-67404 STRASBOURG ILLKIR, FRANCE (Reprint); UNIVERSITE LOUIS PASTEUR, CNRS, INSERM, INST GENET & BIOL MOL & CELLULAIRE, STRUCT BIOL LAB, F-67404 STRASBOURG ILLKIR, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: PROTEINS-STRUCTURE FUNCTION AND GENETICS, (15 AUG 1998) Vol. 32, No. 3, pp. 362-380. Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605 THIRD AVE, NEW YORK, NY 10158-0012. ISSN: 0887-3585.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Histidyl-tRNA synthetase (HisRS) differs from other class II aminoacyl-tRNA synthetases (aaRS) in that it harbors an arginine at a position where the others bind a catalytic Mg2+ ion. In computer experiments, four **mutants** of HisRS from Escherichia coli were engineered by removing the arginine and introducing a Mg2+ ion and residues from seryl-tRNA synthetase (SerRS) that are involved in Mg2+ binding. The **mutants** recreate an active site carboxylate pair conserved in other class II aaRSs, in two possible orders: Glu-Asp or Asp-Glu, replacing Glu-Thr in native HisRS, The **mutants** were simulated by molecular dynamics in complex with histidyl-adenylate. As controls, the native HisRS was simulated in complexes with histidine, histidyl-adenylate, and histidinol. The native structures sampled were in good agreement with experimental structures and biochemical data. The two **mutants** with the Glu-Asp sequence showed significant differences in active site structure and Mg2+ coordination from SerRS. The others were more similar to SerRS, and one of them was analyzed further through simulations in complex with histidine, and His+ATP. The latter complex sampled two Mg2+ positions, depending on the conformation of a loop anchoring the second carboxylate. The lowest energy conformation led to an active site geometry very similar to SerRS, with the principal Mg2+ bridging the alpha- and beta-phosphates, the first carboxylate (Asp) coordinating the ion through a water molecule, and the second (Glu) coordinating it directly. This **mutant** is expected to be catalytically active and suggests a basis for the previously unexplained conservation of the active site Asp-Glu pair in class II aaRSs other than HisRS. Proteins 32:362-380, 1998. (C) 1998 Wiley-Liss, Inc.

L12 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:260104 CAPLUS
DOCUMENT NUMBER: 126:260880
TITLE: 5' nucleases derived from thermostable **DNA polymerases** and their use in a nucleic acid detection method
INVENTOR(S): Dahlberg, James E.; Lyamichev, Victor I.; Brow, Mary Ann D.
PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA

SOURCE: U.S., 93 pp., Cont.-in-part of U.S. 5,541,311.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5614402	A	19970325	US 1994-254359	19940606
US 5422253	A	19950606	US 1992-986330	19921207
US 5541311	A	19960730	US 1993-73384	19930604
US 5837450	A	19981117	US 1995-471066	19950606
US 5843654	A	19981201	US 1995-484956	19950607
US 5719028	A	19980217	US 1997-789079	19970206
US 5888780	A	19990330	US 1997-802233	19970219
US 2003054338	A1	20030320	US 2001-940925	20010828

PRIORITY APPLN. INFO.:

US 1992-986330	A2	19921207
US 1993-73384	A2	19930604
US 1994-254359	A3	19940606
US 1994-337164	B2	19941109
US 1995-402601	A2	19950309
US 1995-484956	A2	19950607
US 1995-520946	A1	19950830
US 1997-789079	A2	19970206
US 1997-802233	A2	19970219
US 2000-655378	A3	20000905

AB Derivs. of thermostable **DNA polymerases** that retain their 5'-nuclease activity but lack polymerase are described for use in a nucleic acid detection system. The nuclease activity cleaves the single-stranded moiety of a Y-shaped structure and so is of use in selected cleavage of reporter sequences in a hybridization assay that includes two 5'-nuclease-dependent cleavage and amplification steps. The presence of the target sequence is demonstrated by the release of the reporter moiety from sequences immobilized on a carrier. The ability of the nuclease activity to cleave such structures was shown by the inability of intact Taq polymerase to amplify a hairpin sequence, although the nuclease-free Stoffel fragment could amplify the target sequence. The prepn. and characterization of a no. of polymerase **mutants** for use in these assays is demonstrated. Specific alterations of the Thermus aquaticus Taq gene wee: a deletion between nucleotides 1601 and 2502 (the end of the coding region), a 4-nucleotide insertion at position 2043, and deletions between nucleotides 1614 and 1848 and between nucleotides 875 and 1778. Three of these derived 5'-nucleases were designated Cleavase BX, Cleavase BB, and Cleavase BN.